REMARKS/ARGUMENTS

35 U.S.C. §103(a).

Claims 1 to 20 were rejected under 35 U.S.C. §103(a) as allegedly obvious over Barker in light of Sadowski et al., (US Pat. No.: 5,885,779) ("Sadowski"), Young (Biology of Reproduction (1998) 58:302-311) ("Young") and Finley et al., (The Yeast Two-Hybrid System, eds P. Bartel, S. Fields, Oxford Unversity Press, (1997) pp. 197-214) ("Finley"), Hagahara et al.. (Nature Medicine (1998) 4:1449-1452), and Schwarze (Science (1999) 285: 1569-1572). Action at page 2-4. As the rejection applies to the claims, Applicants traverse.

Three requirements must be met for a *prima facie* case of obviousness. First, the prior art reference must teach all of the limitations of the claims. M.P.E.P § 2143.03. Second, there must be a motivation to modify the reference or combine the teachings to produce the claimed invention. M.P.E.P. § 2143.01. Third, a reasonable expectation of success is required. M.P.E.P. § 2143.02. The teaching or suggestion to combine and the expectation of success must be both found in the prior art and can not be based on Applicants' disclosure. M.P.E.P. §2143.

A first requirement for establishing a *prima facie* case of obviousness is that the combination of the cited art, taken with the general knowledge in the field, must provide all of the elements of the claimed invention. When a rejection depends on a combination of prior art references, there must be some teaching, suggestion or motivation to combine the references. In re Geiger, 815 USPQ2s 1276, 1278 (Fed. Cir. 1987). Moreover, to support an obviousness rejection the cited references must additionally provide a reasonable expectation of success. In re Vaeck, 20 USPQ2d 1438 (Fed. Cir. 1991), citing In re Dow Chemical Co., 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

The cited reference fails to teach the present invention because it teaches a nonfunctional assay. The Barker can not describe the present claim 1 because, e.g., an agent's ability to modulate a cells accumulation or degradation of a metabolic product literally can not be detected by mimicking a binding inhibition **action** of APC. The use of

the word "action" (how APC works) with reference to using a two hybrid system (Examiner's citation of teachings at column 6, line 53) is in contrast the description in the same paragraph of using described non-two hybrid assays to test compounds that mimic the "effect" (the result of APC activity). The author must be taken at his word. The cited statement can not teach claim 1, inter alia, because it is based on a flawed theory that can not function in practice. The action of APC, as described, e.g., in the present application (e.g., in the two paragraphs starting at page 15, line 24), is to facilitate addition of phosphate groups to β-catenin by glycogen synthase kinase (GSK3β). The action of APC does not involve Tcf or binding interactions with Tcf. The action of APC can not be mimicked by inhibition of β-catenin/Tcf binding because inhibition of binding does not provide β-catenin phosphorylation. This erroneous teaching of Barker can not be cured by addition of any elements from the other cited references. Furthermore, there would be no expectation of success from such defective combinations of references. Because the nonfunctional cited system can not teach the functional system of the present invention, the rejection of present claims based on Barker should be withdrawn.

In addition, the §103 rejection should be withdrawn because the Examiner fails to cite references that alone or in combination provide the present assay system working in a mammalian cell. Rejected claim 1 of the present invention claims screening methods, e.g., with mammalian cells comprising chimeric proteins and an effector gene. Barker describes a Tcf reporter system in mammalian cells (e.g., column 9, line 13) which is not a two-hybrid system. As cited by the Examiner at column 6, line 52, Barker mentions briefly that "... compounds can be tested for the ability to inhibit the binding of .beta.-catenin and Tcf-4, thus mimicking the action of APC. Such a test can be conducted *in vitro* or *in vivo*, for example using a two hybrid assay." However, Barker does not teach a two hybrid assay in mammalian cells, and stable reliable mammalian two hybrid assays were not described in the art at the time. One skilled in the art at the time would have understood the cited statement to suggest practicing the Barker Tcf-responsive reporter as a two hybrid assay *in vitro*, or in combination with yeast two hybrid systems known at the time (e.g., cited references Young or Finley). Those skilled in the art at the time were not taught by Barker, or by any combination of cited references, to practice without unreasonable experimentation the claim

1 limitations of, e.g., detecting altered expression of an effector gene in a mammalian cell comprising chimeric protein screening system components. Claim 1 can not, therefore, be obvious in light of the cited references and the §103 rejection should be withdrawn.

In an additional alternative argument for withdrawal of the §103(a) rejection based on Barker, Applicant believes that the claim 1 limitation wherein a test agent modulates a cell's ability to degrade or accumulate the metabolic products is not present in the cited references. The Examiner (at page 3, paragraph 2, sentence 3 of the Action) states that "Barker et al. considers the Tcf reporter expression [but] not necessarily the beta-catenin degradation product, ..." Apparently, the Examiner considers degradation of the β-catenin metabolic product to be the limitation of claim 1 that is not be described in Barker, yet no citation is provided describing the limitation. Furthermore, the Examiner does not cite references, or even address, the alternate claim 1 limitation concerning accumulation of the metabolic product. In either case, a *prima facie* case of obviousness has not been made because no references have been cited teaching this deficiency in the combination of references. Assuming the Examiner were to provide a reference describing the missing elements, an additional requirement would be for the Examiner to cite a specific suggestion or specific motivation to make such a combination with an expectation of success.

As claim 1 is novel and non-obvious, dependent claims 2 to 20 are also novel and non-obvious. Section §103 rejections of claims 2 to 20 should therefore be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the claims are deemed not to be in condition for allowance after consideration of this Response, a telephone interview with the Examiner is hereby requested. Please telephone the undersigned at (510) 769-3510 to schedule an interview.

QUINE INTELLECTUAL PROPERTY LAW GROUP
P.O. BOX 458, Alameda, CA 94501
Tel: 510 769-3510
Fax: 510 337-7877
PTO Customer No.: **22798**
Deposit Account No.: **50-0893**

Respectfully submitted,

Gary Baker
Reg. No: 41,595

Attachments:

1) A petition to extend the period of response for **2** months;
2) A transmittal sheet;
3) A fee transmittal sheet;
4) A receipt indication postcard.

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